

Comparisons of availability of oral drug formulations for children in France and Canada

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Abstract

Purpose

There are a limited number of adapted oral paediatric drug formulations on the market. Commercially available formulations differ among countries.

Methods

This study compares the number and the characteristics of oral paediatric drug formulations listed on two hospital group purchasing agreement for two large urban area (e.g. Paris and Montreal) valid on April 1st, 2006. Oral paediatric drug formulations included in the study are commercially available (i.e. with a drug identification number issued by the regulatory authority) in at least one adapted formulation (e.g. solution, suspension, powder) that can be used in paediatrics. Radiological contrast media and dietetic products are excluded from the analysis. Data are compared by country, active ingredient, formulation and anatomical therapeutical chemical classification (ATC).

Results

A total of 191 and 151 oral drug formulations and 127 and 94 active ingredients were identified respectively in Paris and Montreal. There are only 47 active ingredients common to both countries. There is a difference in the proportion of oral drug formulations contracted in Paris and Montreal group purchasing. Oral powder in unit dose are commercially available only in France (e.g. 25.1 % of all oral formulation). The distribution of oral formulations per ATC class differs in Paris and Montreal, but both group share the same top three ATC classes (e.g. J – anti-infective for systemic use – 27.7 % vs 25.1 %, N – Nervous system – 31.4 % vs 24.5 %, A – Alimentary tract and metabolism – 21.5 % vs 25.8 %). Based on our clinical and administration experience, the analysis of these differences and specific cases indicates that there are many contributing factors (e.g. market withdrawal, prescribing patterns, commercial interest from manufacturers, dispensing modalities for hospitals, etc.). For instance, oral solution of isoniazid had to be imported from Canada to France in the last year to treat a large cohort of children. Amphotericin B is available in oral solution for the treatment of oral candidosis only in France. An oral solution of ranitidine and phenytoin are available in Canada. A detailed analysis show that notwithstanding these differences, there can be acceptable alternatives (e.g. efferescent tablet for ranitidine in France).

Conclusion

Access to commercially oral drug formulation is an issue in paediatrics. Market globalization should contribute to reduce these differences. A better documentation of differences can contribute to influence drug manufacturer to increase the development and the access to oral drug formulations for children in the world.

Introduction

- Use of unlicensed or off-label drugs to treat children is a widespread phenomenon. (1-4)
- Need to prepare dilutions or to open capsules may increase the risk of life-threatening errors. (5-7)
- There is a limited number of adapted oral paediatric drug formulations on the market.
- The incidence of commercially available oral formulations for children has not been studied to date.
- Objective:** Describe the oral drug formulations available in France and Canada. H opital Robert Debr e (RD), Paris, France and H opital Sainte-Justine (SJ), Montreal, Quebec, Canada were chosen for the comparison.

Method

Source: oral pediatric drug formulations listed on two hospital group purchasing agreements for the two large urban areas (e.g. Paris and Montreal) valid on April 1st, 2006.

Inclusion criteria:

- any oral drug formulations commercially available (i.e. with a Drug Identification Number issued by the regulatory authority),
- available in an adapted formulation (e.g. solution, suspension, powder) that can be used in pediatrics.

Exclusion criteria:

- radiological contrast media,
- dietetic products,
- topical route of administration (e.g. mouthwash).

Drug characteristics: from the Drug Product Database (Health Canada) and the Banque de donn ees sur le m dicament - Th riaque (Groupement d'Int r t Economique - Syst me d'Information sur les Produits de Sant e), but also from direct observation, drug's monograph from the manufacturer. (8-9)

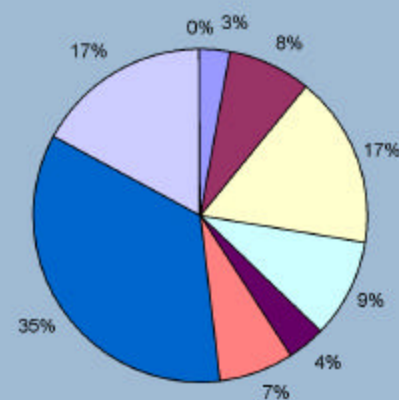
Collected data:

- brand and the generic name product
- anatomical therapeutical chemical classification (ATC),
- drug formulation (ampule, granules, powder, syrup, solution, suspension, elixir),
- dispensing tool (e.g. dropper, graduated spoon or syringe, weight-graduated syringe, specific cup, pouch/packet for powder or a unit-dose formulation).

Statistical tests were χ^2 for comparison of qualitative data.

Results

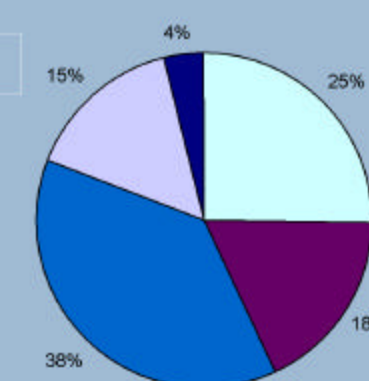
- 191 and 151 oral drug formulations and 127 and 94 active ingredients identified respectively in Paris and Montreal
- Recent antibiotics available in Paris such as voriconazole or linezolid
- Only 47 generic names common to both countries
- Oral solution of isoniazid had to be imported from Canada to Paris in the last year to treat a large cohort of children
- Amphotericin B is available in oral solution for the treatment of oral candidosis only in France
- Oral solution of ranitidine and phenytoin are only available in Canada.



Paris

	Paris		Montr�al	
A-Alimentary tract and metabolism	41	21.5%	39	25.8%
B-Blood and blood forming organs	6	3.1%	4	2.6%
C-Cardiovascular system	6	3.1%	1	0.7%
G-Genito-urinary system and sex hormones	1	0.5%	2	1.3%
H-Systemic hormonal preparations	3	1.6%	1	0.7%
J-Anti-infectives for systemic use	53	27.7%	38	25.1%
L-Antineoplastic and immunomodulator	4	2.1%	3	2.0%
M-Musculo-skeletal system	3	1.6%	3	2.0%
N-Nervous system	60	31.4%	37	24.5%
P-Antiparasitic products	3	1.6%	1	0.7%
R-Respiratory system	8	4.2%	17	11.2%
V-Various	3	1.6%	3	2.0%
Z-No code attributed	0	0.0%	2	1.3%

Oral formulations



Montreal

	Paris		Montr�al		
Dropper	26	13.6%	11	7.3%	P=0.06
Graduated spoon	37	19.3%	5	3.3%	P<0.001
Graduated syringe	49	25.7%	6	4.0%	P<0.001
Weight-graduated measure	7	3.7%	0	0.0%	P=0.02
Specific cup	61	31.9%	6	4.0%	P<0.001
Pouch/packet for powder	48	25.1%	0	0.0%	P<0.001
Unit-dose formulation	63	33.0%	0	0.0%	P=0.004

Discussion

- Limited number** of commercially available oral drug formulations for children
- First study** to evaluate the incidence of commercially available oral drug formulations for children
- Only** comparison of drugs on the two hospital group purchasing agreement
- Many contributing factors:** group purchasing selection, prescribing patterns, hospital practices, market withdrawal, commitment of the industry for drug use in children, regulatory obligations for dispensing
- In France, most **HIV drugs** dispensed through hospitals whereas in Quebec, most dispensed through retail pharmacies. More antiretroviral drugs in solution and powder in Paris than in Montreal
- Unit-dose oral formulations** are available only in Paris and included ampules, granules, powders or solutions in single-dose pack. Also, dispensing tools are provided more frequently by manufacturers in France than in Canada
- Financial obstacles** to drug studies for children, considering the small population targeted and formulation challenges to make acceptable/palatable products. Pharmaceutical industry and their country's based branches should work together to increase the number of oral formulations, but also try to reduce those discrepancies between countries.

Conclusion

There are a limited number of adapted oral pediatric drug formulations on the market. Market globalization should contribute to reduce these differences. This study illustrates the incidence of commercially available oral formulations for children in France and Canada.